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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,157	12/05/2005	Mark Robert Southern	43072-0002US1	1576
23973	7590	07/07/2009	EXAMINER	
DRINKER BIDDLE & REATH			SMITH, CAROLYN L	
ATTN: INTELLECTUAL PROPERTY GROUP			ART UNIT	PAPER NUMBER
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07/07/2009	PAPER			

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/559,157	SOUTHERN ET AL.
	<b>Examiner</b> Carolyn Smith	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 17 April 2009.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-28 is/are pending in the application.
  - 4a) Of the above claim(s) 9-14 and 17-19 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-8, 15, 16 and 20-28 is/are rejected.
- 7) Claim(s) 26 is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 05 December 2005 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 06132006, 12292006
  - 4) Interview Summary (PTO-413) Paper No(s)/Mail Date. \_\_\_\_\_
  - 5) Notice of Informal Patent Application
  - 6) Other: \_\_\_\_\_

**DETAILED ACTION**

Applicant's election of species A (a selected receptor that is a nuclear receptor), G (a step of generating a hydrogen exchange profile that comprises determining both the quantity of isotopic hydrogen and the rate of hydrogen exchange), and I (progressively degrading that comprises fragmenting, identifying, and sequentially terminally degrading using an acid-resistant carboxypeptidase), filed 4/17/09, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 9-14 and 17-19 are withdrawn from consideration as being drawn to non-elected species.

Drawings, filed 12/05/05, are accepted by the Examiner.

The information disclosure statements, filed 6/13/06 and 12/29/06, have been considered by the Examiner.

Claims herein under examination are 1-8, 15-16, and 20-28.

***Specification***

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, such as on page 55, line 22. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

***Claim Objections***

Claim 26 is objected to because of the following informality:

Claim 26 recites “effect” which should be amended to “affect”.

Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 15, and 23-28 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-8, 15, and 23-28 are drawn to a process. A process is statutory subject matter under 35 U.S.C. 101 if: (1) it is tied to a particular machine or apparatus or (2) it transforms an article to a different state or thing (In re Bilski, 88 USPQ2d 1385 Fed. Cir. 2008).

The claimed subject matter is not limited to a particular apparatus or machine. To qualify as a statutory process, the claims should require use of a machine within the steps of the claimed subject matter or require transformation of an article to a different state or thing. Insignificant extra-solution activity in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter (In re Grams 12 USPQ2d 1824 Fed. Cir. 1989). Preamble limitations that require the claimed process to comprise machine implemented steps will not be considered sufficient to convert a process that otherwise

recites only mental steps into statutory subject matter. It is noted that the instant claim 1 recites "generating a hydrogen exchange profile"; however, this step is not a transformation of an article to a different state or thing. It is further noted that claims 1-8, 15, and 23-28 do not explicitly require that the steps of the claimed method are performed on a machine. Applicant is cautioned against introduction of new matter in an amendment.

***Claims Rejected Under 35 U.S.C. § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 15-16, and 20-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 3 and 4 recite the limitation "said computer-assisted modeling" in lines 1-2. There is insufficient antecedent basis for this limitation in the claims as there is no previous mention of this phrase in claims 3 or 4 or claim 1 (from which they depend). Clarification of this issue via clearer claim wording is requested.

Claim 15 recites the limitation "the step of generating a hydrogen exchange profile" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Since "generating a hydrogen exchange profile" is present in steps b, c, and e, it is unclear to which

particular profile the limitation above is referring. Clarification of this issue via clearer claim wording is requested. Claims 16 and 20-28 are also rejected due to their direct or indirect dependency from claim 15.

Claims 24, 26, and 27 recite the limitation "said subfragments" or "said fragments". There is insufficient antecedent basis for these limitations in the claims as there is no previous mention of these limitations in claims 24, 26, 27 or in any claims from which they depend. Clarification of this issue via clearer claim wording is requested. Claims 25 and 28 are also rejected due to their direct or indirect dependency from claim 24 and 27.

Claims 25 and 26 recite the limitation "using" or "the use of" which is vague and indefinite. It is unclear what step or steps are encompassed by this limitation. Clarification of this issue via clearer claim wording is requested.

#### ***Claim Rejections – 35 USC §102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 15, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Fesik et al. (US 5,989,827).

Fesik et al. disclose a method for designing and evaluating one or more compounds which bind to a specific target molecule (i.e. selected receptor) (abstract; col. 1, fourth paragraph). The process includes the steps of identifying a first and second ligand to a specified target using NMR correlation spectroscopy (abstract; col. 1, third paragraph). Fesik et al. further demonstrate the method may be applied to specific receptors related to enzyme activity wherein specific physical/chemical activities of the target are being further evaluated to identify drug leads (pharmacological activity) (col. 1, lines 25-43). Fesik et al. disclose selecting a target molecule (i.e. receptor) and generating a  $^{15}\text{N}/^1\text{H}$  correlation NMR spectrum of the target molecule (col. 3, fourth paragraph), as stated in steps a) and b) of instant claim 1. Fesik et al. disclose the identification of subsequent ligand moieties can be performed in the absence or presence of the first ligand (col. 3, second paragraph). Fesik et al. disclose collecting  $^{15}\text{N}/^1\text{H}$  correlation NMR spectra with the target molecule (i.e. receptor) and first and second ligands in  $\text{H}_2\text{O}/\text{D}_2\text{O}$  (deuterium) solutions which define first and second perturbations of the receptor, using 3D structure to determine spatial orientation of ligands relative to each other and to the target molecule (i.e. receptor), such that isotopic hydrogen and the hydrogen exchange rates of amide molecules throughout the target molecule is measured, both in a ligand free state as well as in the ligand bound states (col. 2, line 31 through col. 4, line 35). In example 4 (col. 21, line 24 through col. 25, line 47), Fesik et al. disclose the hydrogen exchange NMR experiments performed on multiple complexes with the catalytic domain of stromelysin in a ligand-free state, and states bound by one or both of two potential antagonists. The resultant analysis of the hydrogen exchange experiments resulted in further characterization (i.e. comparison) of the selected ligands against the target domain of

stromelysin (col. 24, second paragraph to col. 25, second paragraph). Fesik et al. disclose computer assisted modeling as well as structure determination of the ligand-target complexes, which involved the identification of potential ligands that bind to and alter the conformation of regions of the target molecule (col. 8, second fifth paragraphs; Example 2).

Thus, Fesik et al. anticipate instant claims 1-6, 15 and 23.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 15-16, and 20-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik et al. in view of Smith et al. (Journal of Mass Spectrometry, 1997, Volume 32, pages 135-146).

Fesik et al. describe the limitations of instant claims 1-6, 15, and 23 as discussed in the

102 rejection above. Fesik et al. do not fairly teach or suggest a method of ligand discovery that further employs mass spectroscopy or progressive degradation of products as recited in instant claims 16 and 20-26.

Smith et al. set forth a combination of NMR facilitated hydrogen exchange experiments coupled together with a mass spectroscopic technique involving the progressive degradation of products (abstract and page 138, col. 1, last paragraph to page 144, col. 2, last paragraph), as stated in instant claims 16 and 20. Further Smith et al. teach the use of a range of peptidases that read on the instantly claimed acid-resistant peptidases and combinations thereof (page 138, col. 1, line 42 through page 140, col. 1, line 74). Smith et al. provide for a discussion of the various advantages of investigations involving the determination of hydrogen exchange rates between NMR, mass spectroscopic, and a combination of the two methods. (page 144, col. 1, line 44, through page 145, col. 2, line 25).

It would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use a combination of mass spectroscopic and NMR hydrogen exchange as taught by Smith et al. in combination with compound designing methods as taught by Fesik et al. because Smith et al. teaches that there are advantages to using a combination of NMR and mass spectroscopy methods in measuring hydrogen and deuterium exchange rates (i.e. page 144, col. 1, last paragraph).

Thus, Fesik et al. in view of Smith et al. make obvious claims 1-6, 15-16, and 20-26.

Claims 1-8 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik et al. in view of Shiau et al. (Cell, 1998, Volume 95, pages 927-937).

Fesik et al. describe the limitations of instant claims 1-6, 15, and 23 as discussed in the 102 rejection above. While Fesik et al. teaches a generic method that can be applied to discovering ligands which complex with molecular targets such as receptors, Fesik et al. does not fairly teach or suggest a method of ligand discovery wherein the selected receptors are nuclear receptors as claimed in instant claims 7 and 8.

However, Shiau et al. sets forth a structural basis of antagonism of estrogen receptor/coactivator recognition by a ligand interaction with tamoxifen (abstract and title).

Therefore it would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains to use the compound designing methods as taught by Fesik et al. to further characterize estrogen receptors as disclosed by Shiau et al. because Smith et al. teach that the disclosed techniques provide for an improved method of identifying important characterizing pharmacological features between ligand-receptor complexes (page 934, col. 2, second paragraph).

Thus, Fesik et al. in view of Shiau et al. make obvious claims 1-8 and 15.

### ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28,

1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

July 2, 2009

/Carolyn Smith/  
Primary Examiner  
AU 1631